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Hepatology

Effects of Sho-Saiko-to on hepatocarcinogenesis and 8-hydroxy-2'-deoxyguanosine formation.

Shiota G, Maeta Y, Mukoyama T, Yanagidani A, Udagawa A, Oyama K, Yashima K, Kishimoto Y, Nakai Y, Miura T, Ito H, Murawaki Y, Kawasaki H.

Second Department of Internal Medicine, Tottori University, Yonago, Japan. gshiota@grape.med.tottori-u.ac.jp

Oxidative stress plays an important role in hepatocarcinogenesis. Although Sho-saiko-to (TJ-9), a Japanese herbal medicine which has been recently administered to patients with chronic liver disease in Japan, prevents hepatocarcinogenesis, the mechanism by which TJ-9 protects against cancer development is not fully understood. 8-Hydroxy-2'-deoxyguanosine (8-OHdG), a DNA adduct by reactive oxygen species, is known as a parameter of genetic risk for hepatocarcinogenesis. To clarify whether the preventive effect on hepatocarcinogenesis by TJ-9 is dependent on 8-OHdG, the effect on 8-OHdG levels by TJ-9 was examined by using high-performance liquid chromatography-mass spectrometry (LC-MS) in a diethylnitrosamine (DEN)-induced hepatocarcinogenesis model of male Fisher rats. TJ-9 reduced the number of preneoplastic cells, detected as the glutathione S transferase P (GST-P)-positive hepatocytes, and inhibited the development of liver tumors. TJ-9 also significantly decreased the formation of 8-OHdG, as indicated by LC-MS and immunohistochemical analysis. In addition, ornithine decarboxylase (ODC) activity and the number of proliferating cell nuclear antigen (PCNA)-positive cells were not altered. An electron paramagnetic resonance spin-trapping technique showed that TJ-9 scavenges hydroxyl radicals in a dose-dependent manner. In conclusion, the results of the present study suggest that TJ-9 prevents hepatocarcinogenesis in association with inhibition of 8-OHdG formation.

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